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Previous Correction:
see PCT Gazette No. 27/2004 of 1 July 2004, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CRYSTALLINE FORM OF FATTY ACID AMINE HYDROLASE (FAAH)

(57) Abstract: The present invention is directed to FAAH crystals in complex with the inhibitor methoxyarachidonyl fluorophosphonate (MAFP) and to the use of these crystals to determine the three-dimensional structure of FAAH. This invention id further directed to the use of this structure for the modeling or determination of the structures of related proteins. This invention is further directed to the use of this structure in the pursuit of drug design to identify, characterize, or optimize agents which bind to the active site, substrate channels, product channels, or regulatory sites of FAAH, and to the evaluation of these agents to identify agents which may stimulate, inhibit, relocalize, stabilize, or destabilize FAAH and/or its activity. This invention is further directed to the use of this structure in the development of engineered FAAH variants which display altered solubility, catalytic profiles, or substrate specificity. This invention is further directed to the use of this structure in the development of engineered heterologous proteins with altered membrane tropism.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/36125

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/34; C12N 9/80
US CL : 435/18, 228; 702, 19, 27
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/18, 228; 702, 19, 27

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GIANG et al. Molecular characterization of human and mouse fatty acid amide hydrolysases, Proc. Natl. Acad. Sci. USA March 1997, Vol. 94, pages 2238-2242, see absttract.	1-4, and 6-23
Y	CRAVATT et al. Molecular charachterization of an enzyme that degrades neuromodulatory fatty-acid amides. Nature. 07 November 1996, Vol. 384, pages 83-87, see abstract.	1-4, and 6-23
Y	US 6,271,015 B1 (GILULA et al.) 07 August 2001, see abstract.	1-4, and 6-23
Y	US 6,251,931 B1 (BOGER et al.) 26 June 2001, see abstract.	1-4, and 6-23
Y	US 6,462,054 B1 (BOGER et al.) 08 October 2002, see abstract.	1-4 and 6-23
Y	MAKINO et al. Automated flexible ligand docking method and its application for database Search. J. Comput. Chem. 1997, vol. 18, no. 14, pages 1812-1825, see the abstract.	6-23
A	TOMASSELLI et al. Discovery and design of HIV protease inhibitors and drugs for treatment of AIDS. Advances in Antiviral Drug Design 1996, Vol. 2, pages 173-228.	1-4 and 6-23

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	RICE et al. Single-wavelength anomalous diffraction phasing revisited. Acta Crystallographica Section D: Biological Crystallography 2000, Vol. D56, pages 1413-1420, see abstract.	4
Y	MCDONALD et al. Crystal structure of dimeric human ciliary neurotrophic factor determined by MAD phasing. EMBO J. 1995, Vol. 14, no. 12, pages 2689-2699, see abstract.	4
Y	US 5,221,410 A (Kushner et al.) 22 June 1993, see abstract.	1 and 2
Y	GARAVITO et al. Strategies for crystallizing membrane proteins. Journal of Bioenergetics and Biomembranes. 1996, Vol. 28, No. 1, pages 13-27, see abstract.	1 and 2
A	TAPIAet al. Computer assisted simulation and molecular graphics-methods in molecular design. Molecular Engineering 1994, Vol. 3, pages 377-414, see abstract.	4, and 6-23

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4 and 6-23

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-4, and 6-23, drawn to a crystal of fatty acid amide hydrolase (FAAH), a three dimensional model, a method of determining the three dimensional structure, and a method of identifying an agent that interacts with an internal channel of FAAH.

Group II, claim(s) 5, drawn to a method of determining the molecular structure of molecule or molecular structure whose structure is unknown.

Group III, claim(s) 24 and 25, drawn to a method of identifying an agent that interacts with the SH3-binding domain.

Group IV, claim(s) 26, drawn to drawn to a method of identifying an agent that interacts with the surface helix-loop-helix.

Group V, claim(s) 28-33, drawn to an agent that bind to FAAH and a method of treating pathological condition.

Group VI, claim(s) 34 and 35, drawn to a method of screening an agent for the ability to modulate the activity of FAAH.

Group VII, claim(s) 36, drawn to a method of engineering FAAH variant.

Group VIII, claim(s) 37-39, drawn to a method of altering membrane tropism.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of the invention of Group I is the crystallized FAAH which deferrers from the special technical features of inventions of Groups II-VIII. Group I comprises claims directed to FAAH crystal, a three dimensional model, method of determining the three dimensional model of FAAH (first use), and a method of using the model in identifying compounds that interact with an internal channel of FAAH. The special technical feature of the invention of Group II is the three dimensional model (second use). Also, the special technical feature of the invention of Groups III, IV, and VII are the atomic coordinates or the three dimensional model, and represent a third, forth and fifth use of the model. The special technical feature for the invention of Group V is the molecule determined to bind FAAH, which differs from those of Groups I-IV and VI-VIII. The special technical feature of the invention of Group VI is a solution of FAAH. Finally, the special technical feature of the invention of Group VIII is the membrain-binding domain of FAAH. Thus, inventions I-VIII lack unity of inventon.

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

PCT/US03/36125

STN Search: Medline, Caplus, Scisearch, Lifesci, biosis, and Embase.
WEST: USPT, USOC, EPAB, JPAB, and DWPI.
Sequence Search of SEQ ID NO: 1: U. S. issued patent, PGPUB, PIR,SWISSPORT, and GENESEQ.